TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED / ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371	ATTORNEY'S DOCKET NUMBER P67671US0
	US APPLICATION NO (If known, see 37 CFR 1.5) 10/069128

INTERNATIONAL APPLICATION NO	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PGT/EP00/08545	1 September 2000	3 September 1999

TITLE OF INVENTION

USE OF NATRIURETIC PEPTIDES AS ANTIBIOTICALLY ACTIVE SUBSTANCES FOR THE TREATMENT OF BACTERIAL INFECTIONS

APPLICANT(S) FOR DO/EO/US

Wolf-Georg FORSSMANN, Alexander KRAUSE and Erik MARONDE

Applicant herein submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information.

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. ☒ A proper Demand for Internatl. Preliminary Examination was made by the 19th month from earliest claimed priority date.
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☒ has been transmitted by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)
6. ☒ A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.
8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ A translation of the annexes to the Internatl. Preliminary Examination report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern other document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☒ An assignment document for recording. A separate cover sheet compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.
14. ☐ A substitute specification.
15. ☐ A change of power of attorney and/or address letter.
16. ☒ Other items or information:
    Sequence Listing - 2 Pages

US APPLICATION NO.(If known, see 37 CFR 1.5) 10/069128	INTERNATIONAL APPLICATION NO PCT/EP00/08545	ATTORNEY'S DOCKET NUMBER P67671US0

	CALCULATIONS	PTO USE ONLY
17. ☒ The following fees are submitted:		
Basic National Fee (37 CFR 1.492(a)(1)-(5)):		
Internatl. prelim. examination fee paid to USPTO (37 CFR 1.492 (a) (1)) .. $710.00		
No international preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (2)) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) .. $740.00		
Neither international preliminary examination fee (37 CFR 1.492 (a) (3)) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO) **$1040.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.492 (a) (4)) and all claims satisfied provisions of PCT Article 33(2)-(4) $100.00		
Search Report prepared by the EPO or JPO (37 CFR 1.492 (a) (5)) **$890.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of $130.00 for furnishing the **oath or declaration** later than ☐ **20** ☐ **30** months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

Claims	**Number Filed**	**Number Extra**	Rate		
Total Claims	**7** - 20 =	-0-	x $18.00	$	
Independent Claims	**1** - 3 =	-0-	x $84.00	$	
Multiple Dependent Claim(s) (if applicable)			+ $280.00	$	
TOTAL OF ABOVE CALCULATIONS =				$ 890.00	
Reduction by 1/2 for filing by **small entity**, if applicable. Verified Small Entity statement must also be filed. (Note 37 CFR 1.9, 1.27, 1.28).				$	
SUBTOTAL =				$ 890.00	
Processing fee of $130 for furnishing the **English translation** later than ☐ **20** ☐ **30** months from the earliest claimed priority date (37 CFR 1.492(f))				$	
TOTAL NATIONAL FEE =				$ 890.00	
Fee of $40.00 for recording the enclosed **assignment** (37 CFR 1.21(h)). Assignment must be accompanied by appropriate cover sheet (37 CFR 3.28, 3.31).				$ 40.00	
TOTAL FEES ENCLOSED =				$ 930.00	
				Amt. to be refunded:	$
				Amt. charged:	$

a. ☒ A check in the amount of $ 930.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. **06-1358** in the amount of $ ____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge my account any additional fees set forth in §1.492 during the pendency of this application, or credit any overpayment to Deposit Account No. **06-1358**. A duplicate copy of this sheet is enclosed.

SEND ALL CORRESPONDENCE TO:

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By William E. Player
William E. Player
Reg. No. 31,409

JPH&S 3/95

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Wolf-Georg FORSSMANN et al

Serial No.: New

Filing Date: March 4, 2002

For: USE OF NATRIURETIC PEPTIDES AS ANTIBIOTICALLY ACTIVE SUBSTANCES FOR THE TREATMENT OF BACTERIAL INFECTIONS

PRELIMINARY AMENDMENT

Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

Prior to initial examination, please amend the above-identified application as follows:

IN THE SPECIFICATION

Please insert the following sentence on line 1, immediately following the title:

--This is a 371 of PCT/EP00/08545, filed September 1, 2000, the disclosure of which is incorporated herein by reference.--

IN THE CLAIMS

Please cancel claims 1-7 without prejudice or disclaimer.

Please add new claims 8-14 as found on the following page.

CLAIMS:

8. Use of natriubiotics for the preparation of an antibiotically active agent for the treatment of a pathogenically altered bacterial flora in the gastro-intestinal tract, respiratory and urogenital systems, the skin, and for use in food technology as an auxiliary agent in fermenting processes and as a preservative.

9. The use according to claim 8, wherein said natriubiotics are formulated in amounts of from 1 µg to 1 mg per unit for infusions, ointments, tablets, sprays or sustained release capsules.

10. The use according to claim 8 for the treatment of alterations of the intestinal flora.

11. The use according to claim 8 for the treatment of alterations of microbially induced skin diseases.

12. The use according to claim 8 for the treatment of aberrations of the human vaginal flora.

13. The use according to claim 8 as a preservative for foods or other perishable goods.

14. The use according to claim 8 as an auxiliary agent in industrial fermenting processes, e.g., in beer production, in yogurt production and in sauerkraut production.

REMARKS

The foregoing Preliminary Amendment is requested in order to delete the multiple dependent claims and avoid paying the multiple dependent claims fee.

Early action on the merits is respectfully requested.

Respectfully submitted,

JACOBSON HOLMAN PLLC

By _____
William E. Player
Reg. No. 31,409

400 Seventh Street, N.W.
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Atty. Docket: P67671US0
Date: March 4, 2002
WEP:jrc

SMB

Use of Natriuretic Peptides as Antibiotically Active Substances for the Treatment of Bacterial Infections

The present invention relates to the use of natriuretic peptides (ANP, BNP, CNP and urodilatin) as antibiotically active peptide preparations. The peptides are obtained by chemical peptide synthesis or biotechnological production, and confectioning as a galenically prepared substance for medical and veterinary use as a medicament.

The peptides to which this invention relates are members of the family of natriuretic peptides. The primary structures of atrial natriuretic peptide (ANP) of rats (Flynn et al., 1983), pigs (Forssmann et al., 1983, 1984) and humans (Kangawa and Matsuo, 1984) have been described. The form of ANP which occurs in the kidneys, urodilatin, was first isolated in 1988 by Forssmann et al. (Schulz-Knappe et al., 1988). The homologue of atrial natriuretic peptide (ANP), the brain-type natriuretic peptide (BNP), was first isolated in 1988 by Sudoh et al. To date, an antibiotic activity of natriuretic peptides has not been suggested. To prove antimicrobial activity, a test is preferably performed which is suitable for basic peptides. A useful test for recognizing antibiotic activity is the growth inhibition test of Lehrer et al. (Lehrer et al., J. Immun. Methods, Vol. 137, p. 167, 1991).

It has been the object of the invention to provide antibiotically active agents. This object is achieved by the use of natriuretic peptides (natriubiotics, such as ANP, BNP, CNP and urodilatin) according to claim 1. The dependent claims relate to preferred embodiments of the use according to the invention.

According to the invention, the natriubiotics are used for the preparation of an antibiotically active agent for the treatment of a pathogenically altered bacterial flora in the gastro-intestinal tract, respiratory and urogenital systems, the skin,

and for use in food technology as an auxiliary agent in fermenting processes and as a preservative.

When used as medicaments, the natriubiotics are preferably formulated in amounts of from 1 µg to 1 mg per unit into infusions, ointments, tablets, sprays or sustained release capsules.

The use of natriubiotics according to the invention also comprises the treatment of alterations of the intestinal flora, the treatment of microbially induced skin diseases, the treatment of aberrations of the human vaginal flora. The use of natriubiotics in food technology according to the invention also comprises the use as a preservative for foods or other perishable goods, as an auxiliary agent in industrial fermenting processes, e.g., in beer production, in yogurt production and in sauerkraut production.

Surprisingly, human ANP 99-126 and urodilatin have a growth-inhibiting effect on Gram-positive bacteria, such as *B. subtilis*, *M. luteus* and *S. carnosus*, and on Gram-negative bacteria, such as *E. coli*, *N. cinerea* and *P. fluorescens*, and the yeast *S. cerevisiae*. Also, human BNP-312 has the same growth-inhibiting effect on Gram-positive bacteria, such as *B. subtilis*, *M. luteus* and *S. carnosus*, and on Gram-negative bacteria, such as *E. coli*, *N. cinerea* and *P. fluorescens*, and the yeast *S. cerevisiae*. The growth-modulating property of these specific natriuretic peptides on certain germs has been unequivocally proven for the first time.

By chemical and biotechnological synthesis, the natriuretic peptides can be prepared in a highly pure and biologically active form and employed as a medicament.

The substances which can be used according to the invention, consisting of synthetic and recombinant products, can change the bacterial flora of the intestine, the skin and other bacterially colonized body zones and lead to an improvement of the germ flora in bacterial colonization by misplaced species. Therefore, the isolated pure substances can be used for controlling diarrheas, especially infant diarrheas, i.e., infections of the gastro-intestinal tract, but also of the respiratory system, the urogenital system and in skin infections. The preparations can be used

as additives for foods or as therapeutic agents and serve as auxiliary agents in the production of foods, especially in foods which are prepared by fermentation and other bacterial processes. These preparations are natural preservatives.

In the following, the invention is illustrated by means of Examples and the following Figures to which reference is made in the Examples:

Figure 1 shows a growth inhibition test of ANP

Radial diffusion growth inhibition test with *Streptococcus carnosus* and *N. cinerea* according to Lehrer et al. (Lehrer et al., J. Immun. Methods, Vol. 137, p. 167, 1991). The growth inhibition test is particularly suitable for the detection of antibiotic peptides since a special agarose which does not contain any fixed charged sites was used as the support material instead of the otherwise usual agar-agar. After application of 1 µg of ANP (both germs), inhibition halos can be observed.

Figure 2 shows a growth inhibition test of urodilatin

Radial diffusion growth inhibition test with *Streptococcus carnosus* and *N. cinerea* according to Lehrer et al. (Lehrer et al., J. Immun. Methods, Vol. 137, p. 167, 1991). The growth inhibition test is particularly suitable for the detection of antibiotic peptides since a special agarose which does not contain any fixed charged sites was used as the support material instead of the otherwise usual agar-agar. After application of 1 µg of urodilatin (both germs), inhibition halos can be observed.

Figure 3 shows a growth inhibition test of BNP-32

Radial diffusion growth inhibition test with *Streptococcus carnosus* and *N. cinerea* according to Lehrer et al. (Lehrer et al., J. Immun. Methods, Vol. 137, p. 167, 1991). The growth inhibition test is particularly suitable for the detection of antibiotic peptides since a special agarose which does not contain any fixed charged sites was used as the support material instead of the otherwise usual

agar-agar. After application of 0.1 µg of BNP (both germs), inhibition halos can be observed.

Figure 4 shows a growth inhibition test of CNP

Radial diffusion growth inhibition test with *Streptococcus carnosus* and *N. cinerea* according to Lehrer et al. (Lehrer et al., J. Immun. Methods, Vol. 137, p. 167, 1991). The growth inhibition test is particularly suitable for the detection of antibiotic peptides since a special agarose which does not contain any fixed charged sites was used as the support material instead of the otherwise usual agar-agar. After application of 7 µg (*S. carnosus*) and 11 µg (*N. cinerea*) of CNP, inhibition halos can be observed.

Example 1:

Chemical synthesis of the antibiotically active peptides ANP, BNP, urodilatin and CNP

Strategy of the synthesis of human natriuretic peptides:

For the synthesis of the peptides with the following sequences:

Ser-Leu-Arg-Arg-Ser-Ser-Cys-Phe-Gly-Gly-Arg-Met-Asp-Arg-Ile-Gly-Ala-Gln-Ser-Gly-Leu-Gly-

Cys-Asn-Ser-Phe-Arg-Tyr (ANP/CDD)

Ser-Phe-Lys-Met-Val-Gln-Gly-Ser-Gly-Cys-Phe-Gly-Arg-Lys-Met-Asp-Arg-

Ile-Ser-Ser-SerSer-Gly-Leu-Gly-Cys-Lys-Val-Leu-Arg-Arg-His (BNP)

Gly-Leu-Ser-Lys-Gly-Cys-Phe-Gly-Leu-Lys-Leu-Asp-Arg-Ile-Gly-Ser-Met-Ser-Gly-LeuGly-Cys (CNP)

Thr-Ala-Pro-Arg-Ser-Leu-Arg-Arg-Ser-Ser-Cys-Phe-Gly-Gly-Arg-Met-Asp-Arg-Ile-Gly-Ala-Gln-

Ser-Gly-Leu-Gly-Cys-Asn-Ser-Phe-Arg-Tyr (urodilatin),1

the continuous flow method (Atherton and Sheppard, in "Solid Phase Peptide Synthesis, IRL Press, Oxford 1989) has been used. The peptide sequence mentioned is synthesized by means of an automated peptide synthesis apparatus (Minigen 9050) using Fmoc amino acids. The Fmoc amino acids had L-configuration and were employed in a fourfold excess.

The following amino acid derivatives were used for the synthesis:
Fmoc-Lys (Boc), Fmoc-Arg (Pmc), Fmoc-His (Trt), Fmoc-Glu (OtBu), Fmoc-Ser(tBu), Fmoc-Gln(Trt), Fmoc-Leu, Fmoc-Phe, Fmoc-Ile, Fmoc-Val.
Cys, Gly, Met and Asp are lacking.

The synthesis is performed with a C-terminal amino acid (0.091 mmol of alanine/g of resin) bound to Fmoc-L-Ala-PEG-PS support (Millipore). All coupling processes of amino acid derivatives were performed in the presence of O-(1H-benzotriazole-1-yl)-N,N-N',N'-tetramethyluronium tetrafluoroborate (TBTU), 1-hydroxybenzotriazole and diisopropylethylamine. The following synthesis cycles were used:

- Fmoc deprotection with 20% piperidine in DMF for 10 min;
- washing with DMF for 12 min;
- acylation for 30 min;
- washing with DMF for 8 min.

The synthesis is monitored by continuous UV detection. The synthesis is concluded with the cleavage of the N-terminal Fmoc residue. The resin-bound peptide is washed three times with 50 ml each of isopropanol, glacial acetic acid, isopropanol and diethyl ether, and dried.

The peptides are cleaved from the carrier resin by adding a mixture of TFA-ethanedithiol-water (94:3:3; v/v/v) and precipitated with ether.

The purification of the peptide is effected by reversed-phase HPLC using a C18 column (Vydac, 10 pmm 300 A, 20 x 250 mm, detection at 230 nm). The following mobile solvents were used: eluent A: 0.06% trifluoroacetic acid (TFA); eluent B: 0.06% TFA in acetonitrile/water (4:1). The flow rate is 10 ml/min, and the gradient is as follows: from 20% B to 80% B within 70 min. The pure fractions are pooled and lyophilized.

The purity and identity of the peptides is determined by mass spectrometry (quadrupole electrospray mass spectrometry, Sciex API 111, Perkin Elmer) and sequencing in a gas-phase sequencer (model 470, Applied Biosystems, Weiterstadt) and checked by capillary zone electrophoresis. The biological activity is verified by the growth inhibition test.

Example 2:

Recombinant preparation

The recombinant preparation is effected by usual methods, resulting in a similarly pure peptide for galenic use.

CLAIMS:

1. Use of natriubiotics for the preparation of an antibiotically active agent for the treatment of a pathogenically altered bacterial flora in the gastro-intestinal tract, respiratory and urogenital systems, the skin, and for use in food technology as an auxiliary agent in fermenting processes and as a preservative.

2. The use according to claim 1, wherein said natriubiotics are formulated in amounts of from 1 µg to 1 mg per unit for infusions, ointments, tablets, sprays or sustained release capsules.

3. The use according to claims 1 and/or 2 for the treatment of alterations of the intestinal flora.

4. The use according to claims 1 and/or 2 for the treatment of alterations of microbially induced skin diseases.

5. The use according to claims 1 and/or 2 for the treatment of aberrations of the human vaginal flora.

6. The use according to claims 1 and/or 2 as a preservative for foods or other perishable goods.

7. The use according to claims 1 and/or 2 as an auxiliary agent in industrial fermenting processes, e.g., in beer production, in yogurt production and in sauerkraut production.

Abstract

The present invention relates to antibiotically active natriuretic peptides for use as antibiotically active preparations prepared using biotechnological and recombinant methods and chemical synthesis. The antibiotically active peptides are referred to as natriubiotics. After chemical peptide synthesis, these natriubiotics can be used as human or veterinary medicaments in a suitable galenic formulation or as food additives.

ANP
S.carnosus + N.cinerea

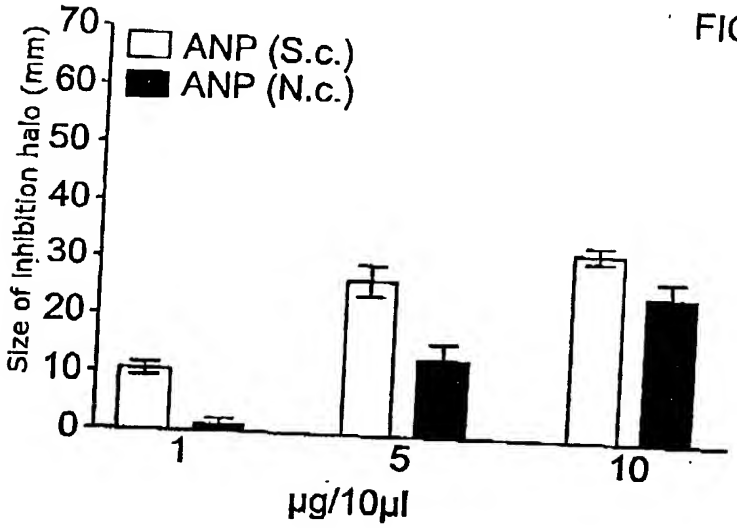

FIG.1

Urodilatin
S.carnosus + N.cinerea

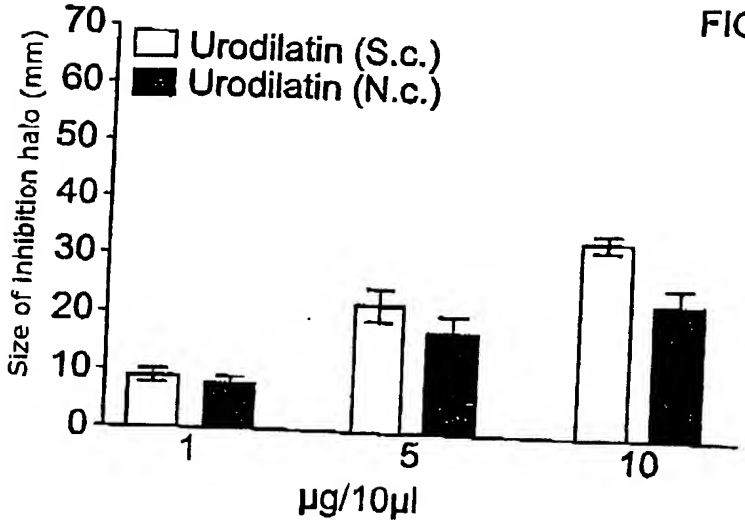

FIG.2

BNP
S.carnosus + N.cinerea

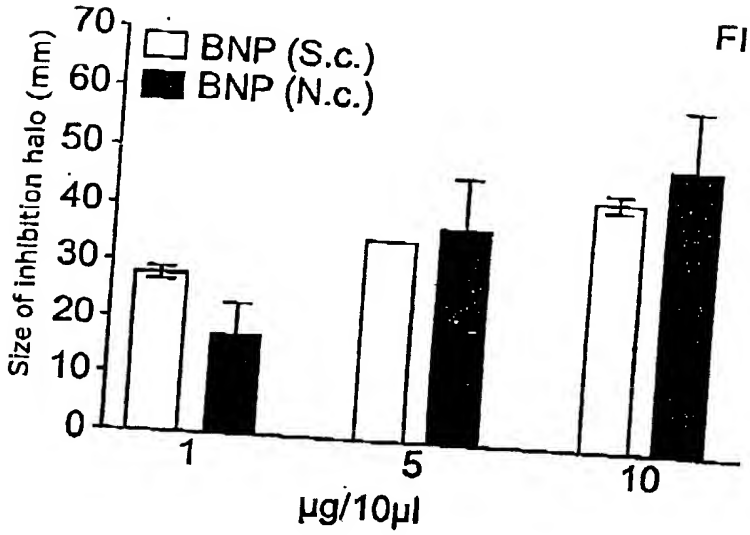

FIG.3

CNP
S.carnosus + N.cinerea

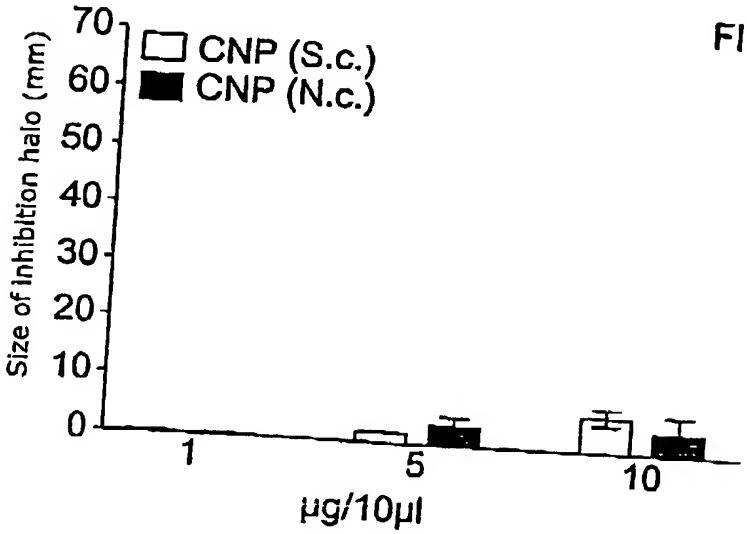

FIG.4

10/069128 - 020402

AND POWER OF ATTORNEY
U.S.A.

ATTORNEYS' DOCKET NO.

-ALL PATENTS, INCLUDING DESIGN
FOR APPLICATION BASED ON PCT; PARIS CONVENTION,
-NON PRIORITY; OR PROVISIONAL APPLICATIONS

101 102

As a below named inventor, I declare that my residence, post office address and citizenship are stated below next to my name. the information given herein is true, that I believe that I am the original, first and sole inventor (if only one name is listed at 201 below), or an original, first and joint inventor (if plural inventors are named below at 201-203, or on additional sheets attached hereto) of the subject matter which is claimed and for which patent is sought on the invention entitled:

USE OF NATRIURETIC PEPTIDES AS ANTIBIOTICALLY ACTIVE SUBSTANCES FOR THE TREATMENT OF BACTERIAL INFECTIONS

which is described and claimed in: [X] PCT International Application No. PCT/EP00/08545 filed September 1, 2000

[ ] the attached specification [ ] the specification in application Serial No. _____ filed _____

(if applicable) and amended on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.
I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.
I hereby claim foreign priority benefits under Title 35, United States Code, §119 (a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s) (Number)	(Country)	(Day/Month/Year Filed)	Priority Claimed Yes	No
199 42 230.3	Germany	September 3, 1999	[X]	[ ]
			[ ]	[ ]
			[ ]	[ ]

103 104

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below:

Application No. _____ Filing Date _____ Application No. _____ Filing Date _____

105

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

(Application Serial No.) (Filing Date) (Status: patented, pending, abandoned)

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorneys (Registration No.) to prosecute this application, receive and act on instructions from my agent, and transact all business in the Patent and Trademark Office connected therewith. HARVEY B. JACOBSON, JR. (20,851); JOHN CLARKE HOLMAN (22,769); MARVIN R. STERN (20,640); ALLEN S. MELSER (27,215); MICHAEL R. SLOBASKY (26,421); JONATHAN L. SCHERER (29,851); IRWIN M. AISENBERG (19,007); WILLIAM E. PLAYER (31,409); YOON S. HAM (45,307) and NATHANIEL A. HUMPHRIES (22,772)

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JACOBSON HOLMAN PROFESSIONAL LIMITED LIABILITY COMPANY 400 SEVENTH STREET, N.W. WASHINGTON, D.C. 20004	**JACOBSON HOLMAN** PROFESSIONAL LIMITED LIABILITY COMPANY

*Inventor(s) name must include at least one unabbreviated first or middle name.

201 FULL NAME * OF INVENTOR	FAMILY NAME: Forssmann	GIVEN NAME: Wolf-Georg		MIDDLE NAME:	
RESIDENCE & CITIZENSHIP	CITY: Hannover	STATE OR FOREIGN COUNTRY: Germany		COUNTRY OF CITIZENSHIP: Germany	
POST OFFICE ADDRESS	POST OFFICE ADDRESS: Blücherstr. 5	CITY: Hannover	STATE OR COUNTRY: Germany		ZIP CODE: 30175
202 FULL NAME * OF INVENTOR	FAMILY NAME: Krause	GIVEN NAME: Alexander		MIDDLE NAME:	
RESIDENCE & CITIZENSHIP	CITY: Rinteln	STATE OR FOREIGN COUNTRY: Germany		COUNTRY OF CITIZENSHIP: Germany	
POST OFFICE ADDRESS	POST OFFICE ADDRESS: Im Obernfeld 21	CITY: Rinteln	STATE OR COUNTRY: Germany		ZIP CODE: 31737
203 FULL NAME * OF INVENTOR	FAMILY NAME: Maronde	GIVEN NAME: Erik		MIDDLE NAME:	
RESIDENCE & CITIZENSHIP	CITY: Hannover	STATE OR FOREIGN COUNTRY: Germany		COUNTRY OF CITIZENSHIP: Germany	
POST OFFICE ADDRESS	POST OFFICE ADDRESS: De-Vries-Hof 3	CITY: Hannover	STATE OR COUNTRY: Germany		ZIP CODE: 30627

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code; and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201	SIGNATURE OF INVENTOR 202*	SIGNATURE OF INVENTOR 203*
DATE 31.01.2002	DATE 31.01.2002	DATE 31.01.2002

[ ] Additional inventors are named on separately numbered sheets attached hereto.

SEQUENCE LISTING

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Krause, Alexander
Maronde, Erik

<120> Use of Natriuretic Peptides as Antibiotically Active Substances for the Treatment of Bacterial Infections

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